REMARKS

Claims 1-4, 7, 8 and 22-25 are all the claims pending in the application. Claims 6-21 are canceled without prejudice, being directed to a non-elected invention.

I. Election/Restrictions

It is noted that the Examiner has acknowledged Applicant's election without traverse of Group II: R^1 and R^2 = H, X=F, Y=-$S(O)_nR^7$ where n=l and R^7 = phenyl group in the reply filed on June 7, 2007.

II. Detailed Action

Claim Rejections - Under 35 USC § 103

1. Claims 1-8 and 22-25 are rejected under 35 USC 103(a) as being unpatentable over Fernandez et al. (US 5,912,248, US '248).

According to the Examiner, US '248 discloses compounds that are positional isomers of the presently claimed compounds and, thus, the presently claimed compounds are *prima facie* obvious over US '248.

For the following reasons, the rejection is overcome.

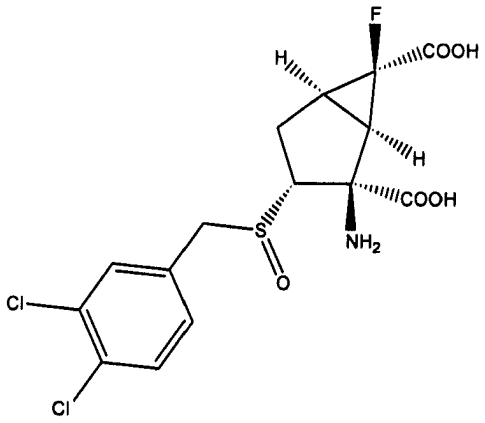
The claims as amended herein recite a 2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivative that has fluorine at the 6-position of the bicyclo ring and that has the Y substituent at the 3-position of the bicyclo ring. In contrast, US '248 discloses a 2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivative that has hydrogen at the 6-position of the bicyclo ring and that has the X-R substituent at the 4-position of the bicyclo ring. Because of these structural differences, the present invention as recited in the amended claims possesses an unexpected advantage as compared to the invention disclosed in US '248 as explained below.

US '248 discloses that the compounds were tested for affinity for metabotropic glutamate receptors as demonstrated by the selective displacement of 1S,3R-ACPD-sensitive [^{3}H]glutamate binding to rat brain cell membranes. US '248 further discloses "[t]he compounds exemplified herein, except for the compound of Example 8, have all been found to have an IC_{50} of less than 10 μM [10,000 nM] in this test. For example, the compound of Example 1 was found to have an IC_{50} of 0.242 μM [242 nM] in this test." See column 9, lines 58-62.

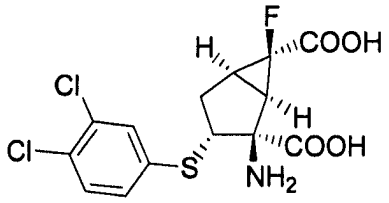
On the other hand, the present specification teaches that "compounds 1 to 58 described in table 1 [], showed a low IC_{50} value of below 200nM, which indicates a strong binding action on mGluR2 receptors, when measured as described in the test example of the present invention." See page 68, lines 1-3.

In order to further demonstrate the unexpectedly superior properties of the presently claimed compounds, Applicant submits herewith a Declaration under 37 CFR §1.132. The Declaration describes an experiment in which the activity to regulate Group II metabotropic glutamate receptors of Compound Nos. 10 and 12 described in the specification of the above-identified application was compared with the activity of the compound of Example 1 in US '248. The compound of Example 1 in US '248 has a structure similar to the structures of Compound Nos. 10 and 12, except that the compound of Example 1 of US '248 has hydrogen, not fluorine, at the 6-position of the bicyclo ring and has an X-R substituent at the 4-position of the bicyclo ring rather than the Y substituent at the 3-position of the bicyclo ring.

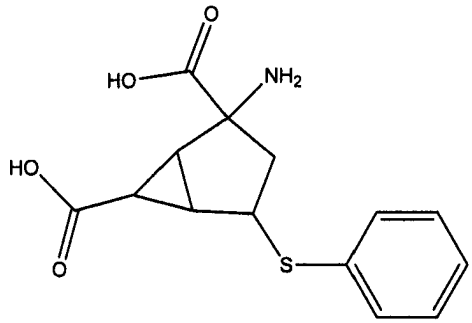
The chemical structures of the three compounds are shown below.



Compound No. 10 of the present invention



Compound No. 12 of the present invention



2-amino-4-(phenylthio)bicyclo[3.1.0]hexane-2,6-dicarboxylic acid

Example 1 in US '248.

The results are shown in the following Table 1, which is the same as in the Declaration.

Table 1

	Example 1 in US 5,912,248	Compound No. 10	Compound No. 12
IC_{50}	242 nM*1)	12 nM	3.9 nM

*1) This data is based on the description in US '248.

As is apparent from the data in Table 1, Compound Nos. 10 and 12 have binding activities about 20 and 60 times as high, respectively, as the compound of Example 1 in US '248.

Accordingly, the present invention as recited in the amended claims possesses an unexpected advantage as compared to the compounds of US '248.

Accordingly, the Examiner is requested to reconsider and remove this rejection.

2. Elected Group II compounds are rejected under 35 USC 103(a) as being unpatentable over Fernandez et al. (US 5,912,248, US '248) in view of Silverman, The Organic Chemistry of Drug Design and Drug Action.

The Examiner cites Silverman as teaching that H and F are equivalent in terms of substituents on drugs.

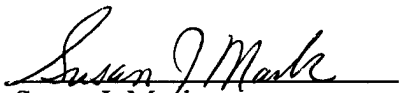
This rejection is overcome for the same reasons the rejection over US '248 is overcome. Accordingly, the Examiner is requested, respectfully, to reconsider and remove this rejection.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the

Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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Date: November 2, 2007